ARTICLE IN PRESS
EI-03543; No of Pages 20

Environment International xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Review article

Measuring biomarkers in wastewater as a new source of epidemiological information: Current state and future perspectives

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ARTICLE INFO

Article history:
Received 28 October 2016
Received in revised form 12 December 2016
Accepted 16 December 2016
Available online xxxx

Keywords:
Wastewater
Epidemiology
Biomarker
Consumption
Exposure
Population

ABSTRACT

The information obtained from the chemical analysis of specific human excretion products (biomarkers) in urban wastewater can be used to estimate the exposure or consumption of the population under investigation to a defined substance. A proper biomarker can provide relevant information about lifestyle habits, health and wellbeing, but its selection is not an easy task as it should fulfil several specific requirements in order to be successfully employed. This paper aims to summarize the current knowledge related to the most relevant biomarkers used so far. In addition, some potential wastewater biomarkers that could be used for future applications were evaluated. For this purpose, representative chemical classes have been chosen and grouped in four main categories: (i) those that provide estimates of lifestyle factors and substance use, (ii) those used to estimate the exposure to toxicants present in the environment and food, (iii) those that have the potential to provide information about public health and illness and (iv) those used to estimate the population size. To facilitate the evaluation of the eligibility of a compound as a biomarker, information, when available, on stability in urine and wastewater and pharmacokinetic data (i.e. metabolism and urinary excretion profile) has been reviewed. Finally, several needs and recommendations for future research are proposed.

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http://dx.doi.org/10.1016/j.envint.2016.12.016
0160-4120/© 2016 Published by Elsevier Ltd.

Contents

1. Introduction

Relevant epidemiological information about lifestyle habits, public health and wellbeing can be obtained from the chemical analysis of urban wastewater. This approach, called *wastewater-based epidemiology* (WBE), is based on the analysis of specific human metabolic excretion products (biomarkers) in wastewater as indicators of consumption or exposure of the population served by the sewer network under investigation to different substances. WBE has been successfully applied as a suitable approach for the estimation of illicit drugs consumption (Ort et al., 2014; Thomaidis et al., 2016; Thomas et al., 2012; van Nuijs et al., 2011a; Zuccato et al., 2008), but it has also recently been employed to assess other lifestyle-related factors such as alcohol (Rodríguez-Álvarez et al., 2015; Ryu et al., 2016), nicotine (Castiglioni et al., 2015b; Lopes et al., 2014; Rodríguez-Álvarez et al., 2014b), caffeine (Senta et al., 2015a) and new psychoactive substances (NPS) (Kinyua et al., 2015; Reid et al., 2014a; van Nuijs et al., 2014). WBE has also been applied to verify community-wide exposure to endocrine disruptors and antimicrobial agents in personal care and household products (O'Brien et al., 2015; Rydevik et al., 2015). The broad range of information that can be gathered from wastewater opens up the possibility of expanding WBE to other human biomarkers providing clues about diet, health, diseases and exposure to contaminants. For example by linking exposure to environmental or food contaminants with health outcomes such as diabetes or cancer.

In general, a human biomarker can be an endogenous compound (produced naturally in the body) or a metabolite of a xenobiotic/exogenous substance (produced through metabolic processes after intentional consumption of a substance, accidental exposure to environmental contaminants, as well as through diet or ingestion of a substance). Biomarkers can be classified on the basis of their function as biomarkers of exposure (compounds that give information about substances consumed or ingested) and biomarkers of effect (indicators of measurable changes or alterations in an organism that can be associated with health problems or wellbeing) and on the basis of biological nature (e.g. metabolites, hormones), or of the disease they can indicate (e.g. cardiovascular biomarkers, obesity biomarkers) (Pischon, 2009).

The selection of a specific biomarker is not an easy task, as it needs to satisfy different criteria (Fig. 1) (Castiglioni and Gracia-Lor, 2015; Gracia-Lor et al., 2016). From a WBE perspective, a suitable biomarker must be excreted mainly via urine and concentration levels in urine should be at least in the μg/L range to ensure its detection in raw wastewater after dilution (Chen et al., 2014).

A biomarker should also be sufficiently stable in wastewater during the transport (in-sewer stability) from the input (i.e. toilet) to the sampling point and during sampling, storage and analysis (in-sample stability) (McCall et al., 2016a). In wastewater biomarkers can undergo further transformation due to microbial activity (Mardal and Meyer, 2014) and/or sorption to particulate matter (Baker and Kasprzyk-Hordern, 2011; Daughton, 2012a; McCall et al., 2016a). The fate of biomarkers in the sewer can be also predicted by using mathematical models to simulate physicochemical and microbial processes (Bisceglia and Lippa, 2014; McCall et al., 2016b; Ramin et al., 2016). It is important to note that biomarker transformation pathways in the sewer might be different from human metabolic pathways.

Furthermore, a biomarker should preferably be specific to the compound under investigation and unique to human metabolism, thus ensuring that its presence only derives from human excretion and not from exogenous sources (Daughton, 2012b). Therefore, pharmacokinetic data on human metabolism are necessary but unfortunately this

Please cite this article as: Gracia-Lor, E., et al., Measuring biomarkers in wastewater as a new source of epidemiological information: Current state and future perspectives, Environ Int (2016), http://dx.doi.org/10.1016/j.envint.2016.12.016